PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2004/035831	27.10.2004	05.11.2003

International Patent Classification (IPC) or both national classification and IPC
A61K39/385, A61K47/48, A61K31/70

Applicant
THE GOVERNMENT OF THE UNITED STATES OF AMERICA...

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2004/035831

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 42-76,79 (with respect to IA)

because:

☒ the said international application, or the said claims Nos. 42-76,79 (with respect to IA) relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	6-11, 14, 16-19, 22, 23, 30, 31, 34, 41, 44-53, 55-59, 65, 66, 69-71, 77-79
	No:	Claims	1-5, 12, 13, 15, 20, 21, 24-29, 32, 33, 36-40, 42, 43, 54, 60-64, 67, 68, and 72-76
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-79
Industrial applicability (IA)	Yes:	Claims	1-41, 77, 78
	No:	Claims	

2. Citations and explanations

see separate sheet

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (SEPARATE SHEET)

International application No.

PCT/US2004/035831

Re item III.

Claims 42-76 and 79 relate to subject-matter considered by this Authority to be covered by the provisions of R. 67.1(iv) PCT, namely to methods of treatment of the human or animal body by therapy. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Art. 34(4)(a)(I) PCT).

Re item V.

1. Reference is made to the following documents:
   - D1: WO 02/32404 A (CONSEJO SUPERIOR DE INVESTIGACIONES CIENTIFICAS; KIDDLE, SIMON, JOHN;) 25 April 2002 (2002-04-25)
   - D2: BARCHI JOSEPH J JR ET AL: "Synthesis and properties of carbohydrate- and glycopeptide-bearing nanoparticles." ABSTRACTS OF PAPERS AMERICAN CHEMICAL SOCIETY, vol. 226, no. 1-2, 2003, page CARB 40 & 226TH ACS (AMERICAN CHEMICAL SOCIETY) NATIONAL MEETING; NEW YORK, NY, USA; SEPTEMBER 07-11, 2003 ISSN: 0065-7727
   - D3: HAKOMORI S: "ABERRANT GLYCOSYLATION IN TUMORS AND TUMOR-ASSOCIATED CARBOHYDRATE ANTIGENS" ADVANCES IN CANCER RESEARCH, ACADEMIC PRESS, LONDON, GB, vol. 52, 1989, pages 257-331
   - D4: GLINSKY VLADISLAV V ET AL: "The role of Thomsen-Friedenreich antigen in adhesion of human breast and prostate cancer cells to the endothelium" CANCER RESEARCH, vol. 61, no. 12, 15 June 2001 (2001-06-15), pages 4851-4857

2. *Novelty (Art. 33(2) PCT):*

2.1 D1 (p. 1, l. 4-10; p. 7, l. 24 - p. 8, l. 14; p. 14, l. 15-28; claims 26-27; Fig. 1) and D2 (abstract) disclose methods of preparing antigen-nanoparticle conjugates wherein a plurality of tumour-associated carbohydrateantigens is attached to the surface of a nanoparticle. D1 and D2 thus destroy the novelty of claim 1.

2.2 D1 (supra; claim 1) and D2 (supra) also disclose the antigen-nanoparticle conjugate

according to claim 12 thereby anticipating said claim.

2.3 D1 (supra) explicitly and D2 (supra) implicitly anticipate the subject-matter of claims 42 and 43 as they disclose a method of inhibiting metastasis using said antigen-nanoparticle conjugates or of inhibiting the tumour cell binding to lectin-bearing endothelial cells ie metastasis.

2.4 The additional features suggested by claims 2-5, 13, 15, 20, 21, 24-29, 32, 33, 36-40, 54, 60-64, 67, 68, and 72-76 are also explicitly or implicitly disclosed by D1 (supra; claims 2-4, 11, 15; p. 3, l. 22 -p. 8, l. 28) and thus do not establish novelty.

2.5 The subject-matter of claims 6-11, 14, 16-19, 22, 23, 30, 31, 34, 41, 44-53, 55-59, 65, 66, 69-71 and 77-79 is novel as the combination of features suggested therein is not disclosed in the prior art.

3. *Inventive step (Art. 33(3) PCT):*

3.1 Claims 14, 16, 17, 51-53 and 77-79 refer to specific tumour-associated carbohydrate antigens, well-known to the skilled person (cf. e.g. D3 and D4). The said tumour-associated carbohydrate antigens are arbitrarily selected and do not bring about any surprising technical effect when putting the teaching of D1 or D2 into practice. Hence, the subject-matter of said claims does not establish an inventive step.

3.2 The additional features suggested by claims 6-11, 18, 19, 22, 23, 30, 31, 34, 35, 41, 44-50, 55-59, 65, 66 and 69-71 refer to routine modifications of the antigen-nanoparticles, of the method of preparing the said or of using them according to D1. These modifications are arbitrary and as not resulting in any surprising technical effect they do not establish an inventive step.

4. *Industrial applicability (Art. 33(4) PCT):*

4.1 For the assessment of the present claims 42-76 and 79 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for

example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

4.2 Industrial applicability of the subject-matter of claims 1-41, 77 and 78 is acknowledged (Art. 33(4) PCT).

5. *Clarity and conciseness (Art. 6 PCT):*

5.1 The subject-matter of claims 42 and 43 is indistinguishable. Hence, one of said claims is superfluous.

5.2 Claims 70-76 define parameters of at least a portion of the nanoparticles or antigen-nanoparticle conjugates referred to. As the said portion is not defined the scope of said claims is rendered unclear.

5.3 The term "carbohydrate antigens specifically expressible on a tumour cell surface" used in claims 1, 12 and 43 is vague and unclear, thereby rendering the scope of said claims undeterminable.

5.4 The tumour-associated carbohydrate antigens referred to in claims 77-79 are not defined in structural terms, thereby leaving the scope of said claims undeterminable.